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When Tocilizumab Became the only Weapon, while the rest of Weapons do not save a Young COVID-19 Patient

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Abstract

Background: The world today is suffering from the pandemic of COVID 19, many cases reported in Iraq since 25th of February 2020. Although, majorities were mild symptoms, however, mortality is recorded. Cytokine storm is devastating sequel that could end in death. This study is aimed to report the cytokine storm features and its management.

Case Presentation: An 18 years old male, who lives in Najaf, Iraq, suffered from fever, cough, severe dyspnea, his test was positive for COVID19. During hospitalization, although he was on the recommended therapy, herapidly deteriorated, had hematuria, tachycardia and hypotension with features of Cytokine storm. For the first time in IRAQ, biological drug (ACTEMRAR) was given with dramatic response after failure of other therapies.

Conclusion: COVID19 in IRAQ could affect any age group, regardless the risk factors and immunity state, usual drugs not always could save patients, biological agent should be available as a life saver.

Keywords: Cytokine storm; COVID 19; Actemra

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Introduction

A few weeks ago, the world witnessed the global pandemic of the novel Virus Corona (COVID-19). It invaded most of the globe, and still, taking more than 225,000 people's lives [1]. Causing a major breach in health systems that were believed to be exemplary, and showed the great imbalance in the defences against this type of epidemic worldwide [2]. Coronaviruses are a large family of single positive-stranded, enveloped RNA viruses that can infect many animal species and humans. Human coronaviruses can be divided based on their pathogenicity. The types with high pathogenicity including SARS-CoV, MERS-CoV, and current novel SARS-CoV2 [3]. Cross-species transmission is the most likely model of the initial transmission from bat to human. The initial transfer believed to have happened in Wuhan, China [4].

Iraq reported first case in Najaf in 25th of February 2020, till now, more than 2000 infected cases [5]. The classical symptoms of the disease are spectrum including: fever, shortness of breath, dry cough, sore throat, fatigue, diarrhoea and body ache, however, some patients had more serious complications like renal impairment, respiratory and serious cardiac illness [6].

The estimated mortality rate is about 3.7%. This figure is very much higher than the estimated death rate after infection with usual seasonal influenza (<0.1%) [7] The death rates and severity of the infection differ according to the people and the possibility of having the risk factors

that cause death more than others [8].

Many studies have instructed that the immune reaction the so called 'the Cytokine storm' is the reason for the rapid deterioration of the body's systems, including, cytokine release syndrome (CRS) and macrophage activating syndrome (MAS) leading to Adult respiratory distress (ARDS).

Cytokine storms have proven with a poor outcome in patients by the significant rise in the level of D-dimer, the level of the serum Ferritin as well as reduced level of platelets [9].

The increasing level of D-Dimer in addition to other coagulation markers point towards coagulation process. Many therapeutic line used for treating patients with cytokine storm including steroids [10], intravenous immune globulin [11], and anticoagulants [12] and antimalarial [13]. However, there are many studies that are completed or under completion that indicates the orientation towards biological treatments to treat the cases of cytokine storms in a CRS and MAS cases [14].

Clinical studies have shown the safety of this agent in the treatment of Cytokine storms for other cases such as rheumatoid arthritis and giant cell tissue [15].

The FDA, recently, approved Tocilizumab for severely ill COVID19 patients [16]. Drugs for those diseases, since, despite the astronomical



injury figures for COVID19, but so far, there is no control study on the safety of this treatment and its success rate.

Roche announced its participation with American research centres at the beginning of this month in a controlled study on the use of this drug for the treatment of corona disease emerging under the name of the COVACTA study [17].

In the light of the previous literatures, we present this case.

Case Presentation

H. A. is an 18 year old male, from a rural decent, working in a central public hospital in Najaf city as cleaning Service employee.

He presented in 17th of April with fever and cough worsening for preceding four days, he had no any significant past medical history only for a mild seasonal allergic bronchitis, on empiric therapy. He denied any direct exposure to patients with similar complaints. Since many cases reported in the area, he was referred for the infectious disease hospital for a suspicion of COVID19.

He admitted to the emergency department in the afternoon. He was complaining from severe nausea, vomiting, and haematuria. On examination he was well-built young age male looks dyspnoeic, on oxygen mask his SPO₂=93%, his pulse reaching 145 BPM regular small volume, his blood pressure was 110/70 mmHg, with maculo-papular rash all over his body (Figure 1). More in chest and abdomen. His temperature was 40.4°C. Local chest examination revealed wheezes and scattered crepitation, other abdominal examination was normal, his cardiac examination was not significant, he was alert and fully conscious part of body examination was negative.



Figure 1: Maculo-papular rash in the chest and upper abdomen.

Investigations taken including nasopharyngeal swab for PCR (Polymerase Chain Reaction) that was positive for COVID19. Chest X ray was not significant. CT-scan in the same day was negative (Figure 2). His blood test showed WBC count 9870/ul, with 6.8% was lymphocytes, the platelets count was 119.000/ul, his fasting glucose level was 160

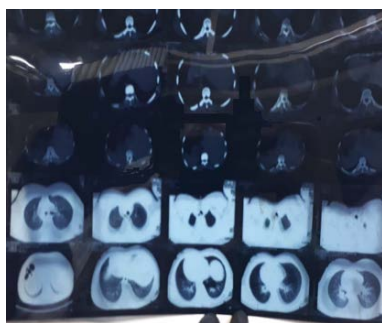


Figure 2: CT scan of chest, no significant changes apart from mild left side pleural effusion.

mg/dl, Serum ferritin and D-dimer were upper normal. He received the supportive therapy including intravenous saline, antipyretics, and antiemetics. At night his condition persist with features of toxemia, increasing tachycardia and fever, fluid and antibiotic given intravenously in addition to cold compresses. In the next day morning the condition became worse, look toxic, severe nausea and frequent vomiting, poor oral take and irritability and diarrhoea. Fever persist about 40°C, pulse 130=BPM, SPO₂=93%,

He received in addition to previous medications-Hydroxychlorquin 200 mg tablets twice daily and subcutaneous Enoxaparin 6000IU twice daily.

His condition deteriorated farther rapidly, worsening dyspnoea, nausea, vomiting, irritability, confusion and tachycardia, his pulse was 137BPM, blood pressure dropped to BP 80/60mmHg, fever reaching 40.5°C, mildly responding for medical therapy.

D-Dimer became 1282 ng/ml, S.Ferritin 530 ng/ml that is five times more than previous readings. Blood picture revealed high ESR (70mm/hr) with low platelets (110 per10e3).

Electrocardiography (ECG) shows inferior and lateral T-wave inversion (Figure 3). Echocardiography revealed dilated right side, moderate tricuspid regurgitation with Right Ventricular systolic pressure (RVSP) 65 mmHg, Ultrasound was normal apart from bilateral mild pleural effusion more on left side. For the above finding the condition labelled as acytokinestorm.

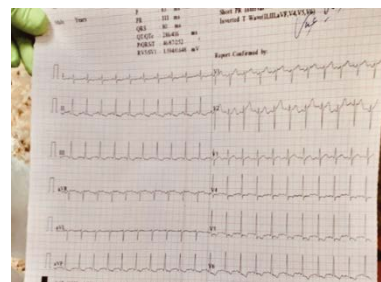


Figure 3: ECG shows tachycardia, T wave inversion in lateral wall, normal Q-T interval.

Fortunately the drug Tocilizumab (Actemra) 20mg/ml solusio was available as a charity donation. The patient was lucky for that. Discussion with a local committee, and decision was taken to administer Tocilizumab (Actemra) 8mg/Kg, infusion over one hour.

Shortly, after completion of the mentioned dose, the patient responded very well, dramatically felt much better, features of toxemia became less, orientation better, and his pulse reduced to 135 beat per minute then few hours reduced 115 (Figure 4). Fever subsided, its evolution in and the normal temperature remained normal till day of discharge (Figure 5).

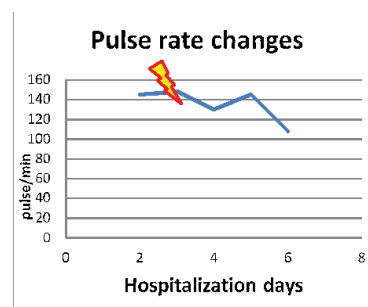


Figure 4: The pulse rate before and after Actemra.

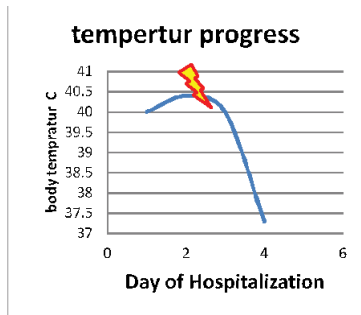


Figure 5: The temperature before and after Actemra.

Couple of hours later after the Actemra injection, blood pressure increased to normal after being in a shock state (Figure 6).

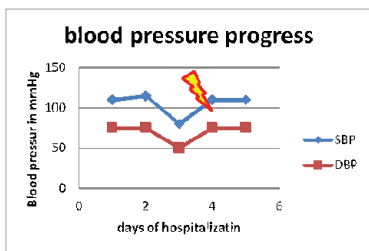


Figure 6: Blood pressure improvement after Actemra injection.

The patient general condition Improved, nausea and vomiting stopped, appetite regained and the patient asking for discharge.

In the second day, blood investigation revealed the following:

The liver function persist few day elevated then return to normal ever (Figure 7).

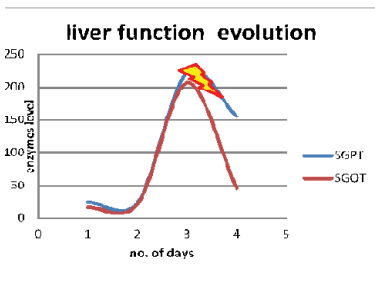


Figure 7: Liver function test, persistent elevation for two days after Actemra injection.

Renal function test, although there was a slight decrement in the renal function, with slight increased blood urea, but had returned normal later (Figure 8), however haematuria persist few days and disappeared later.

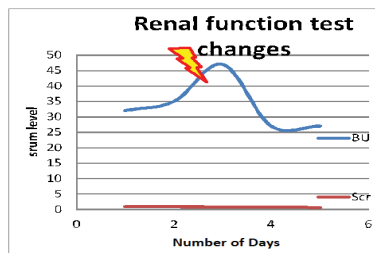


Figure 8: Renal function, slight increased urea during cytokine storm, but returned normal after Actemra injection.

The lymphocyte count and differential started to increase toward normal, which is very important features of recovery from a cytokine storm (Figure 9).

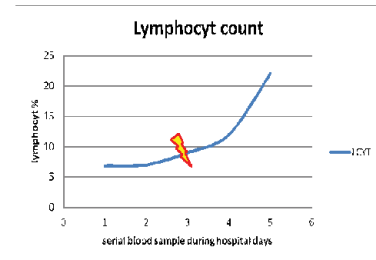


Figure 9: Lymphocyte differential count, was very low then returned normal after Actemra.

The biochemical markers during the cytokinestorm (D-Dimer, S.Ferritin and platelets count reduction) although they were high, before Actemra however, all readings returned towards normality (Figure 10).

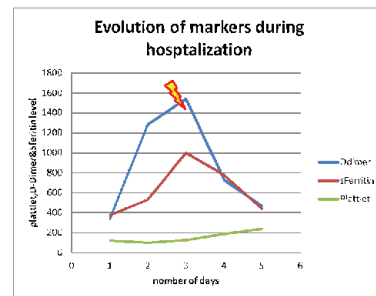


Figure 10: Demonstrate the sharp decline in D-Dimer (blue line) and S.Ferritin (red line), with increasing level of platelets (green line).

The cardio-respiratory derangement duo to cytokine storm reflected as a dilated right ventricular ,tricuspid regurgitation gradient and increased pulmonary pressure that's detected with Echocardiography, after receiving Actemra the extent of overload is reduce greatly (Figure 11).

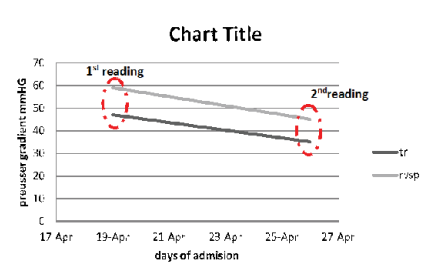


Figure 11: The echocardiographic changes pre (1st reading) and post therapy (2nd reading). the severity of Tricuspid valve regurgitation gradient (tr) and the Right ventricular pressure (RVSP) are reduced after Actemra which represent improvement in cardio-pulmonary-circulation.

Discussion

The previous scenario is similar to other world COVID19 cases that deterioration might occur in the later stages of the disease or in the process of recovery caused by acute respiratory distress syndrome and multiple-organ failure occurred rapidly and death within a short time. Cytokine storm is considered to be one of the major etiologies [18]. Evidence found that the increase cytokines can warn the turning of patients infected with the COVID19 into severe pneumonia [19].



Cardiac complication are recorded even in young patients with serious presentations [20]. Price limitation is a real barrier since doses may expense 2470USD for one patient

Conclusion

Every effort should be paid to save patients with COVID 19, since deterioration might occur rapidly. Cytokine storm is a night mare for both patients and personnel. Tocilizumab should be available to save patients with cytokine storm. If it weren't there, we would have witnessed the youngest COVID-19 mortality in Iraq.

References

1. World Health Organization (2019) Coronavirus disease (COVID-19) pandemic, Switzerland.
2. World Health Organization (2020) WHO releases guidelines to help countries maintain essential health services during the COVID-19 pandemic, Switzerland.
3. Weiss SR, Navas-Martin S (2005) Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. *Microbiol Mol Biol Rev* 69: 635-664.
4. Ge XY, Li JL, Yang XL, Chmura AA, Zhu G, et al. (2013) Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. *Nature* 503: 535-538.
5. United Nations Iraq (2020) Iraq reports the highest COVID-19 case fatality since February, Iraq.
6. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, et al. (2020) Clinical Characteristics of Coronavirus Disease 2019 in China. *N Engl J Med* 382: 1708-1720.
7. Lazzarini M, Putoto G (2020) COVID-19 in Italy: momentous decisions and many uncertainties. *Lancet* 8.
8. Centers for Disease Control and Prevention (2020) Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed Coronavirus disease 2019-COVID-NET, 14 States, March 1-30, 2020. *Morbidity and Mortality Weekly Report* 69: 458-464.
9. Wang W, He J, Lie p, Huang I, Wu S, et al. (2020) The definition and risks of Cytokine Release Syndrome-Like in 11 COVID-19-infected Pneumonia critically ill patients: Disease Characteristics and Retrospective Analysis. *medRxiv*.
10. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, et al. (2020) COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet* 395: 1033-1034.
11. Schnur MB (2020) Is COVID-19 fueled by a Cytokine Storm?. *Lippincott Nursing Center, United States*.
12. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, et al. (2020) Coagulopathy and antiphospholipid antibodies in patient with COVID-19. *N Engl J Med* 382: e38.
13. Cortegiani A, Ingoglia G, Ippolito M, Giarratano A, Einav S (2020) A systematic review on the efficacy and safety of Chloroquine for the treatment of COVID-19. *J Crit Care* 57: 279-283.
14. Shimabukuro-Vornhagen A, Gödel P, Subklewe M, Stemmler HJ, Schlöber HA, et al. Cytokine release syndrome. *J Immunother Cancer* 6: 56.
15. Ahn SS, Jung SM, Song JJ, Park YB, Park JY, et al. (2018) Safety of tocilizumab in rheumatoid arthritis patients with resolved hepatitis B virus infection: data from real-world experience. *Yonsei Med J* 59: 452-456.
16. Tocilizumab in the Treatment of Coronavirus Induced Disease (COVID-19) (CORON-ACT). University Hospital Inselspital: NCT04335071.
17. Parsons L (2020) FDA approves Roche's Actemra COVID-19 trial.
18. Ye Q, Wang B, Mao J (2020) The pathogenesis and treatment of the 'Cytokine Storm' in COVID-19. *J Infect* 80: 607-613.
19. Lipin G (2020) Increase of two serum cytokines may predict severity of COVID-19. *Xinhua*.
20. Kim IC, Kim JY, Kim HA, Han S (2020) COVID-19-related myocarditis in a 21-year-old female patient. *Eur Heart J* 41: 1859.